Tuberculosis in Pregnancy

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- Any opinions expressed are my own and not of any of my sponsors.

Overview

- Global TB burden and epidemiology
- Impact on maternal-child health outcomes
- Screening for active and latent TB infection (LTBI) in pregnancy/ postpartum
- Treatment

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Learning Objectives

- To discuss the epidemiology and clinical outcomes of TB in pregnancy
- To discuss screening and diagnosis for TB in pregnancy
- To discuss treatment of TB in pregnancy and highlight some research gaps

Historical perspective

- Hippocrates
  - Pregnancy improves the outcome of pthisis (tuberculosis)
- 1850-1920s
  - TB harmful during pregnancy, termination recommended
- Modern era
  - First-line drugs safe, treat TB
  - MDR TB, abortion offered

What is the burden of TB in pregnancy?

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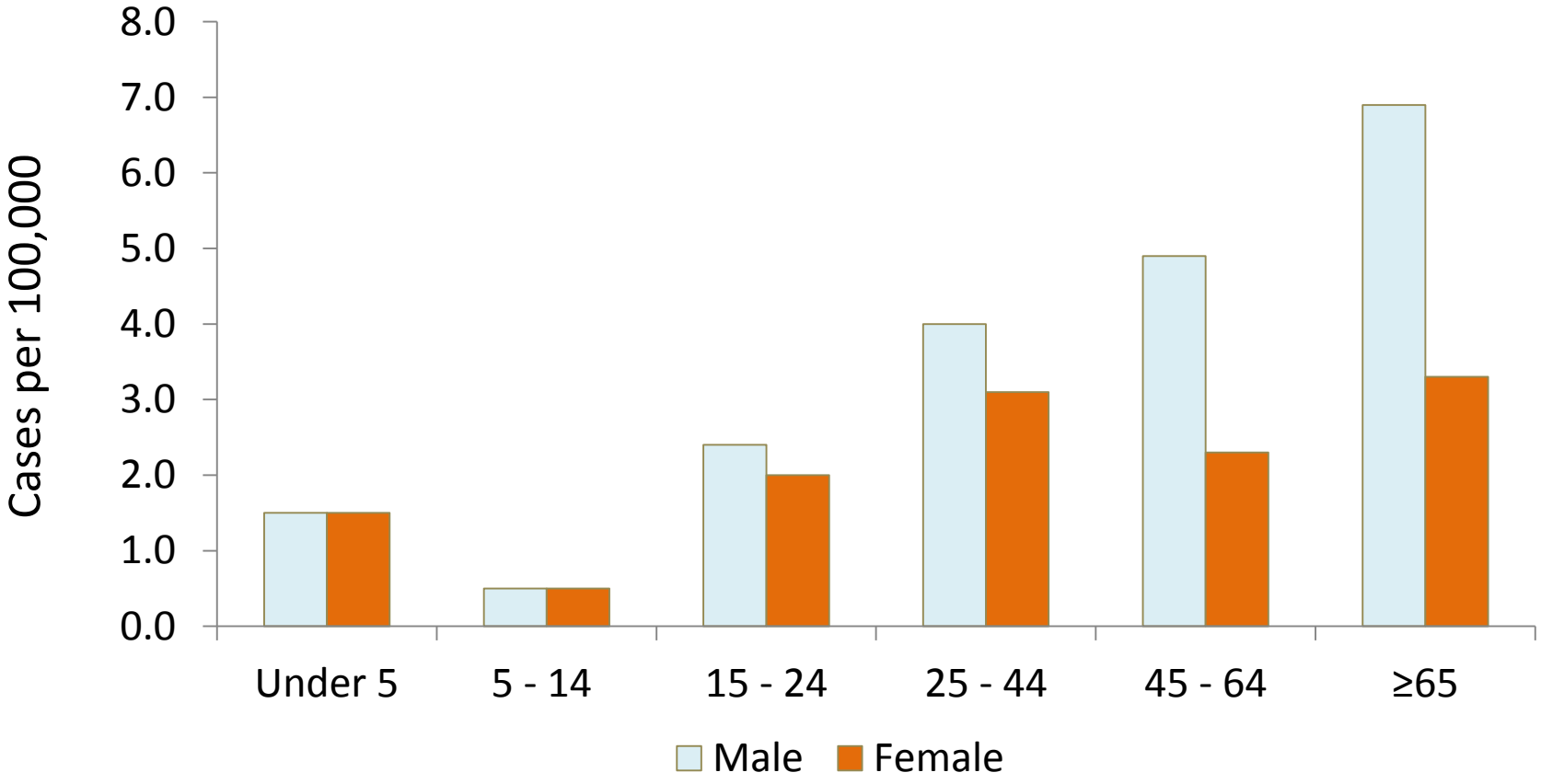
World Health Organization

TUBERCULOSIS IN WOMEN

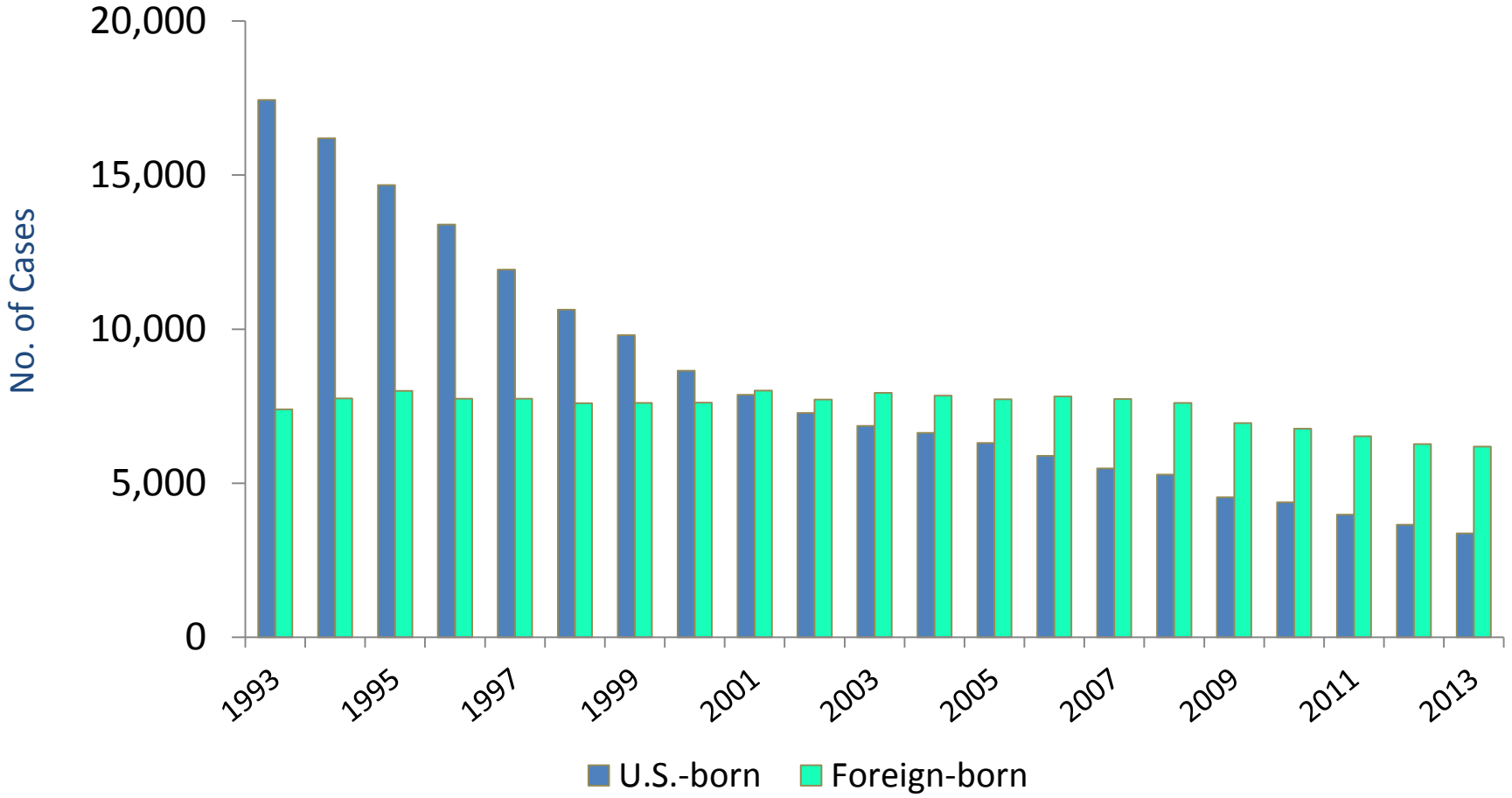
- 2014
  - >500,000,000 latently infected
  - 3.3 million with active TB (37% of global burden)
  - 510,000 died (180,000 HIV-infected)
  - 50% of HIV-related TB deaths
  - 67% of cases Africa and SE Asia
  - More than 50% of female TB cases went undetected

WHO Global TB Report 2014

TB Case Rates by Age Group and Sex, United States, 2013

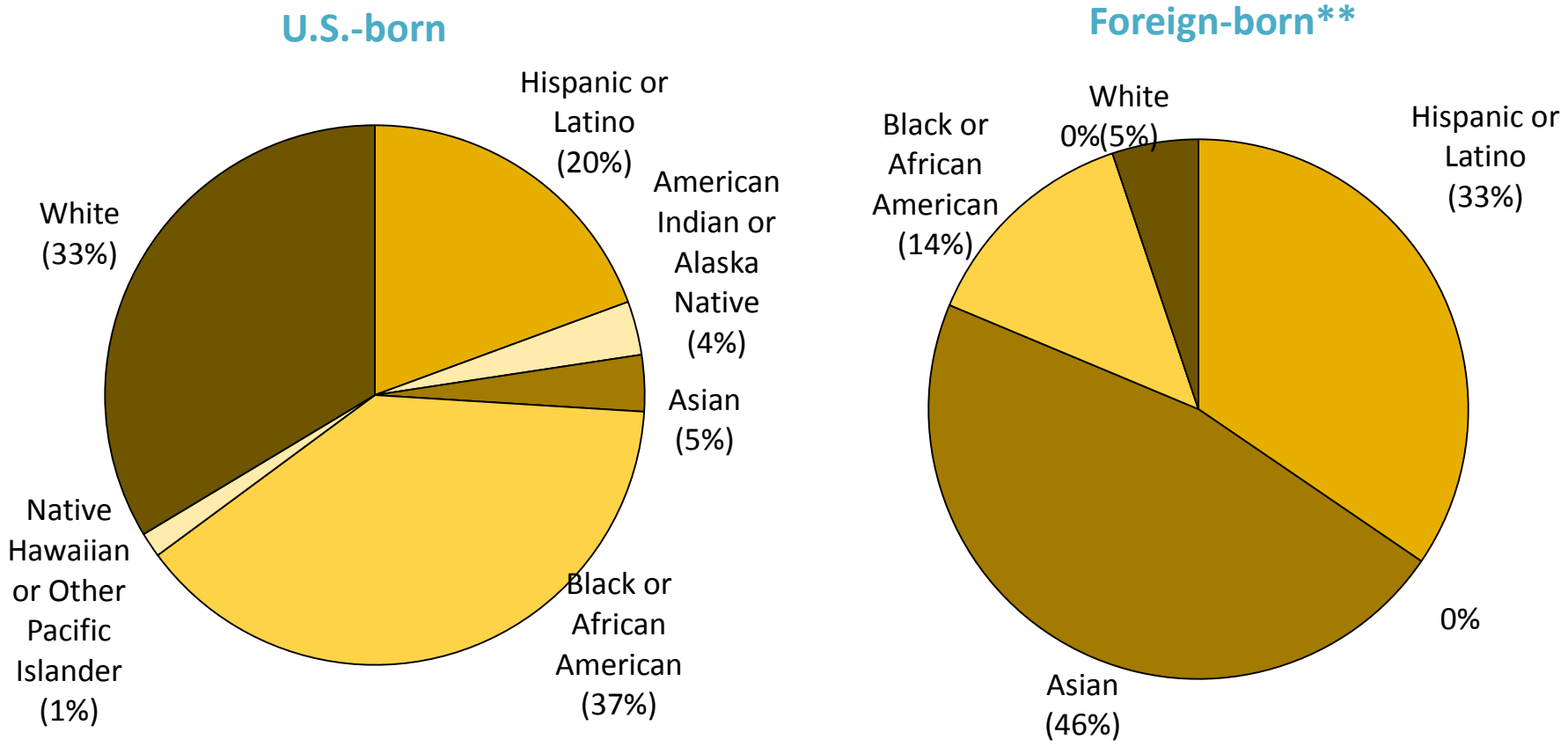


Number of TB Cases in U.S.-born vs. Foreign-born Persons, United States, 1993–2013*



*Updated as of June 11, 2014.

Reported TB Cases by Origin and Race/Ethnicity,* United States, 2013



*All races are non-Hispanic. Persons reporting two or more races accounted for less than 1% of all cases.

** American Indian or Alaska Native and Native Hawaiian or Other Pacific Islander accounted for less than 1% of foreign-born cases and are not shown.

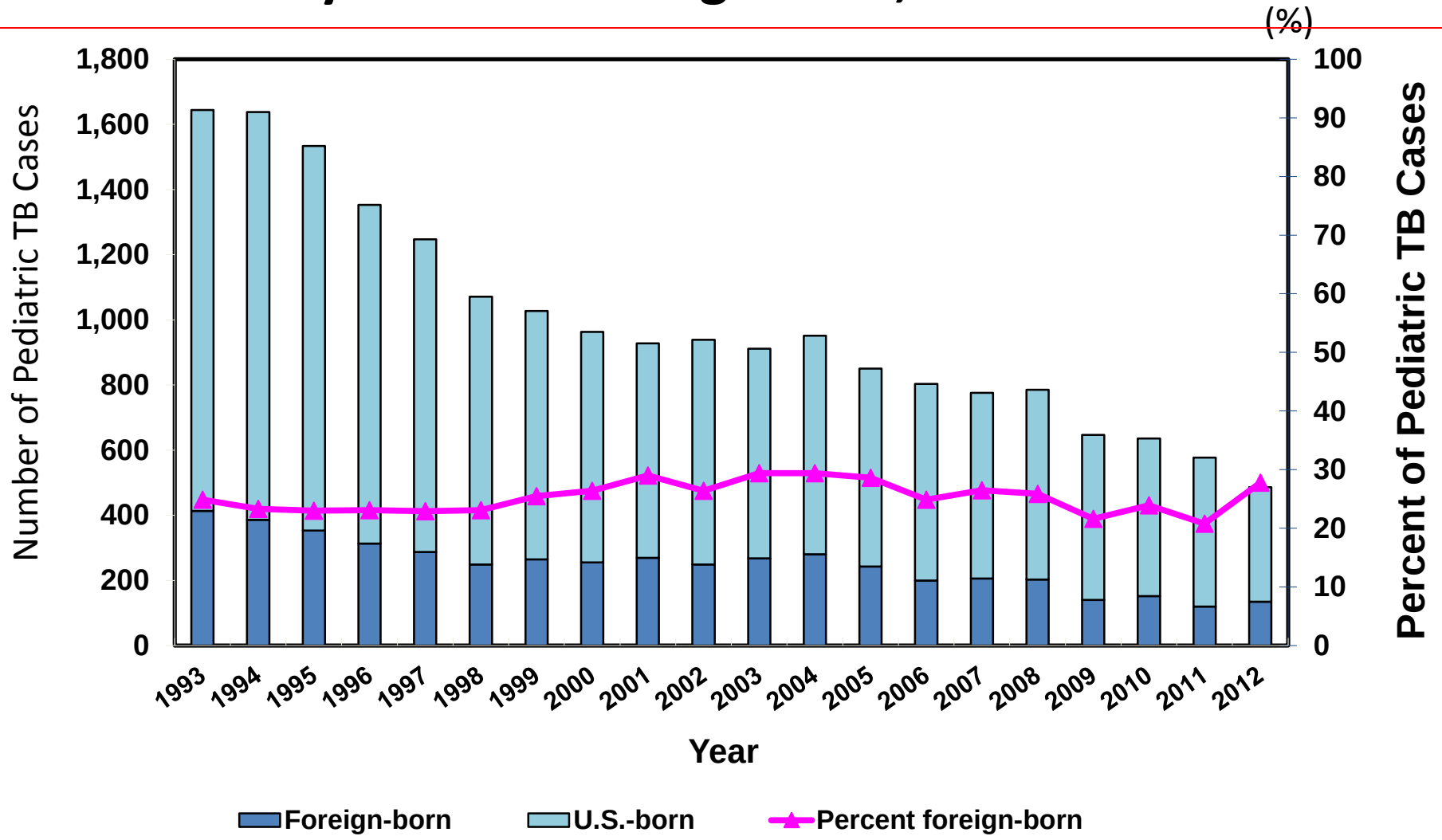
Pediatric TB—Background

- **Definition of pediatric tuberculosis (TB):**
  TB disease in a person < 15 years old

- **In 2012:**
  - **9,945 TB cases were reported among all age groups**
    - **486 (4.9%) were pediatric**

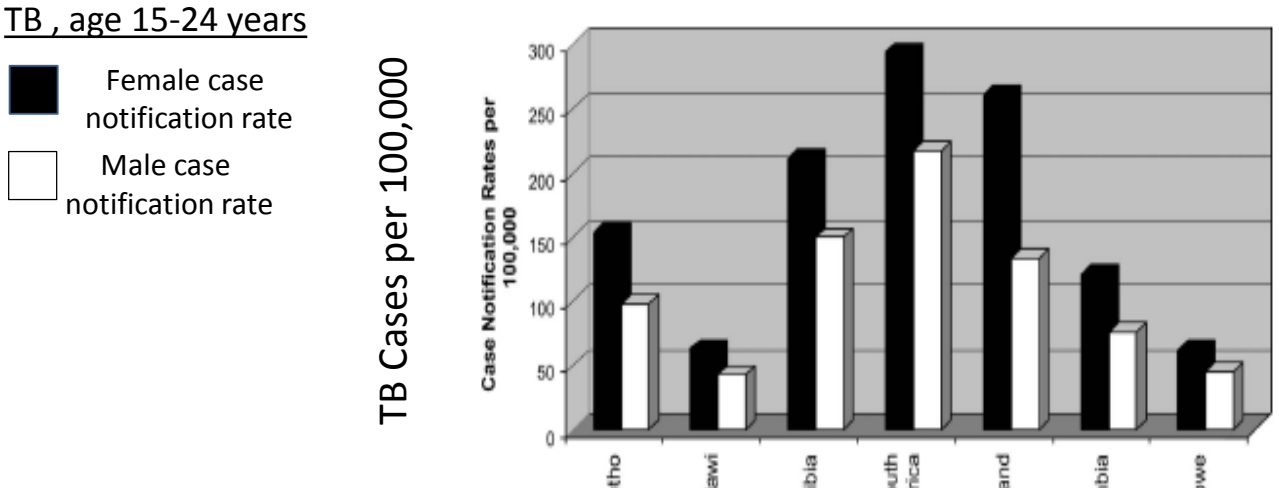
Age Group	N	Percent out of all age groups
0 – 4 years	260	2.6%
5 – 14 years	226	2.3%

Number and Percent of Pediatric TB Cases by U.S. and Foreign Birth, 1993–2012



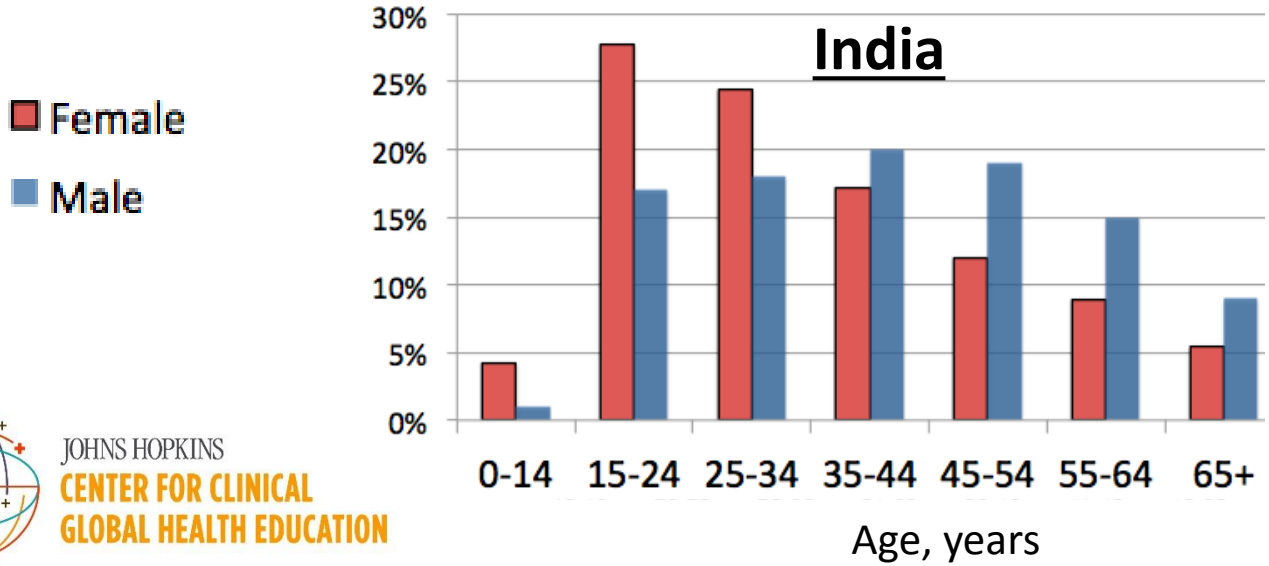
Peak TB incidence in women of reproductive age irrespective of HIV

Sub-Saharan African Women



Deluca JAIDS 2009

Women 15-24 years have TB rates 1.5-2-fold higher than men



RNTCP: Gender differentials in TB control 2004

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Extrapulmonary TB (EPTB) more prevalent in women

- US 253,299 cases, 73.6% were PTB and 18.7% were EPTB. Compared with PTB, EPTB was associated with female sex (OR 1.7; 95% CI, 1.7-1.8)

- Being female identified as independent risk factor for EPTB

(Lin IJTLD 2009; Yang CID 2004; Kingkaew IJID 2009; Lowieke EID 2006)

Prevalence of TB in pregnancy

- No national reporting for high or low burden countries
- Data based on individual screening studies

Active TB

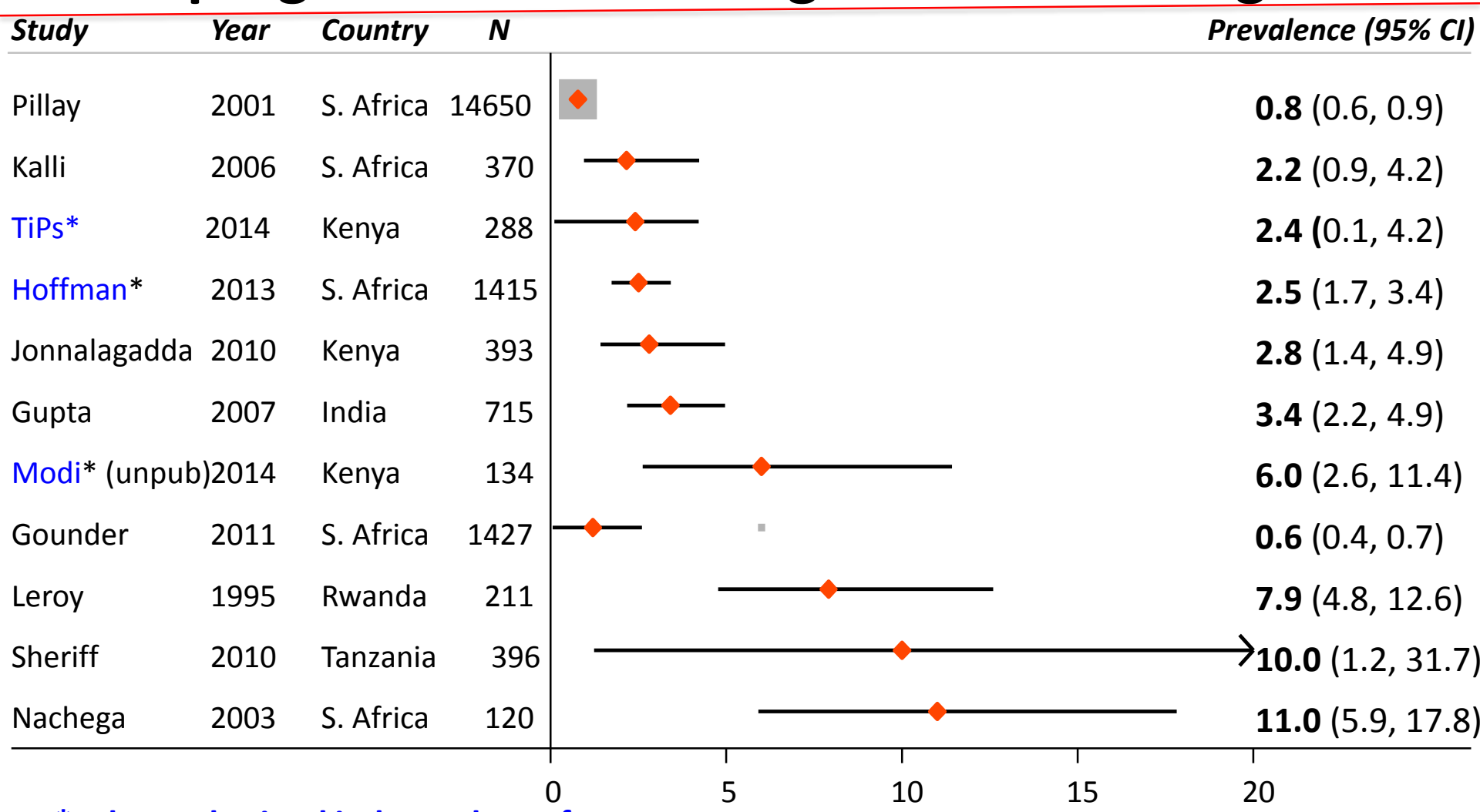
Study Site	HIV-negative	HIV-positive
Low burden countries	0.06-0.25%	1%
High-burden countries	0.07-0.53%	0.69-11%

Latent TB

Study Site	HIV-negative	HIV-positive
Low burden countries	10-23%	11-26%
High-burden countries	18-34%	21-49%

Mathad & Gupta, CID 2012

Prevalence of TB disease in HIV-infected pregnant women in high burden settings



***culture obtained independent of symptoms**

Prevalence: 0.6-11%

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Slide courtesy of Sylvia LaCourse, Univ of Washington

Global estimate of TB in pregnancy

	Mean (95% uncertainty range)	Rate per 1000 pregnant women (95% uncertainty range)	Percentage of global burden
All countries combined	216 500 (192 100–247 000)	2·1 (1·8–2·4)	..
African Region	89 400 (74 200–110 500)	3·6 (3·0–4·5)	41%
Region of the Americas	4800 (3900–6000)	0·4 (0·3–0·5)	2%
Eastern Mediterranean Region	28 500 (19 700–41 900)	2·3 (1·6–3·4)	13%
European Region	4900 (3800–6300)	0·6 (0·5–0·8)	2%
South-East Asia Region	67 500 (52 000–87 100)	2·4 (1·9–3·1)	31%
Western Pacific Region	21 400 (19 400–23 700)	1·1 (1·0–1·2)	10%

Table 2: Total number of active tuberculosis cases in pregnant women, rate per 1000 pregnant women and percentage of global burden by WHO region and combined

Based on total population, crude birth rate, age distribution, TB case notification by age/sex

Sugarman, Lancet Global Health 2014

Impact of Maternal TB on maternal-infant outcomes?

Risk of complications in pregnancy TB vs. no TB

Maternal complications

- Pre-eclampsia & eclampsia (2 fold)
- Vaginal bleeding (2 fold)
- Hospitalization (12 fold)
- Miscarriage (10 fold)

Jana Int J Gyn Obstet 1994
Jana NEJM 1999
Chin HC BJOG 2010
Bjerkedal 1975

Bothalmley 2001
Pillay Lancet ID 2000;
Mathad CID 2012

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TB Disease is a Leading Cause of Maternal Mortality in Women With and Without HIV Co-infection

- 50,518 deliveries in Durban, South Africa 1996-1998; there were 101 maternal deaths for overall mortality 200 per 100,000 deliveries.
- Mortality by HIV infection and TB disease status:

	Maternal Mortality Rates (per 100,000 deliveries)	
HIV Infection Status	All	Tuberculosis Status
HIV-infected	323	12,170
HIV-uninfected	149	3,850

RR of maternal death was 3.2 higher for TB/HIV vs TB alone

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Khan M et al. AIDS 2001;15:1857-63

Risk of complications in pregnancy TB vs. no TB

Fetal and infant complications

- Fetal death (increased)
- Low birth weight (2 fold)
- Lower Apgar scores
- Prematurity (2 fold)
- Small for gestational age (2 fold)
- Perinatal death (increased)
- congenital TB (rare)
- Increased HIV transmission (2 fold)

Jana Int J Gyn Obstet 1994
Jana NEJM 1999
Chin HC BJOG 2010

Khan AIDS 2001;
Pillay Lancet ID 2000;
Gupta JID 2011

MTCT of TB

- In utero
  - Hematogenous dissemination via the umbilical vein
  - Aspiration/ingestion of infected amniotic fluid
- Intrapartum
  - Aspiration/ingestion of infected amniotic fluid or genital secretions
- Postpartum
  - Inhalation/ingestion of respiratory droplets from the mother
  - Ingestion of infected breast milk

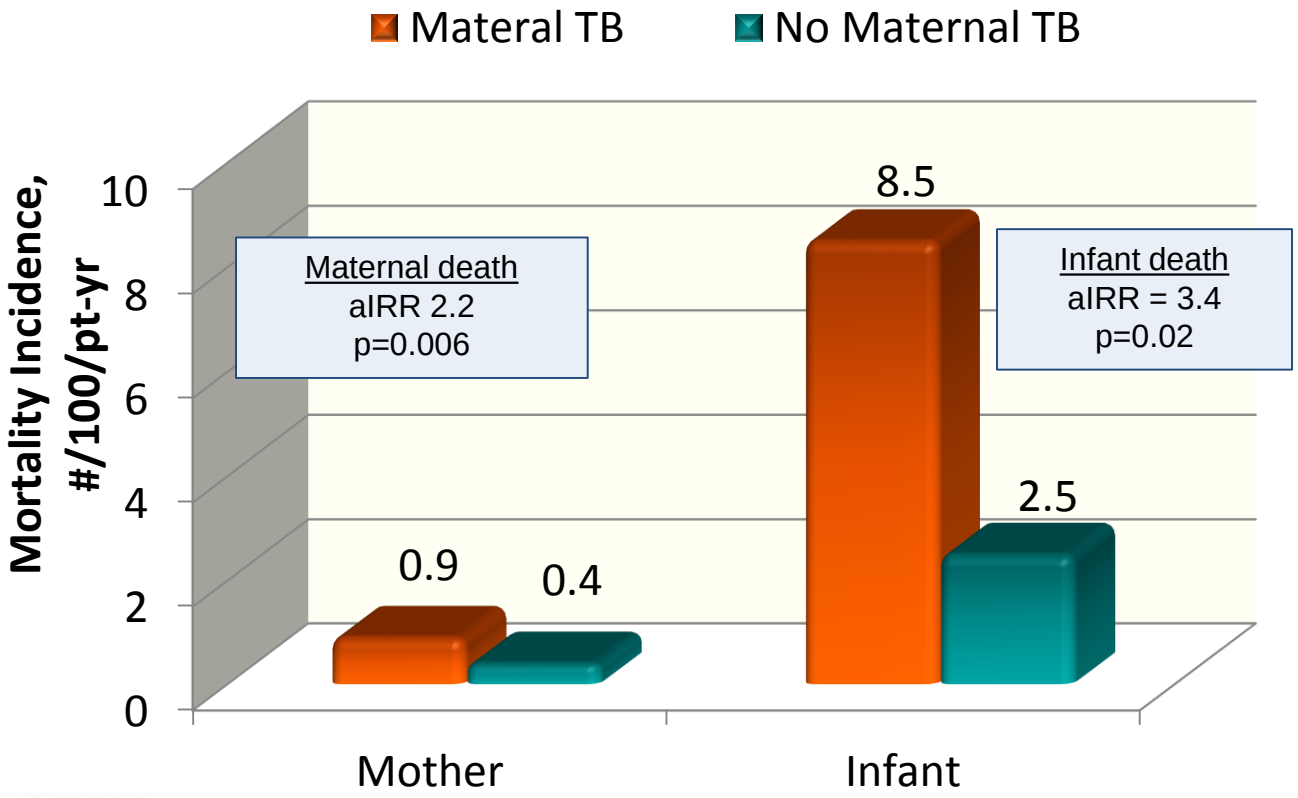
Congenital TB

- Rare, ≈300 reports in the literature
- Old data suggest prevalence <1% for offspring of untreated mothers (Beitzke 1935,Hedvall 1953)
- Risk factors include maternal disseminated TB and diagnosis made close to delivery, maternal genital tract TB
- Cantwell criteria for diagnosis (infant proven TB lesions and one of the following: 1) 1st wk of life; 2) hepatic complex/granulomas; 3) maternal genital tract or TB in placenta; 4) exclusion of postnatal contacts (including hospital staff)

Smith 2002; Starke 1997; Cantwell 1994; Whittaker 2008

Postpartum TB important causes maternal and infant mortality in HIV infected women

- HIV-infected mothers have 10-fold increase in TB.
- Maternal TB/HIV increased risk of **postpartum mortality by 2.2 fold and probability of infant death by 3.4 fold**.



715 HIV-infected pregnant women in Pune, India

TB incidence 5/100 pt-yr (24 of 715 HIV+ women)

Gupta A et al. Clin Infect Dis 2007;45:241-9

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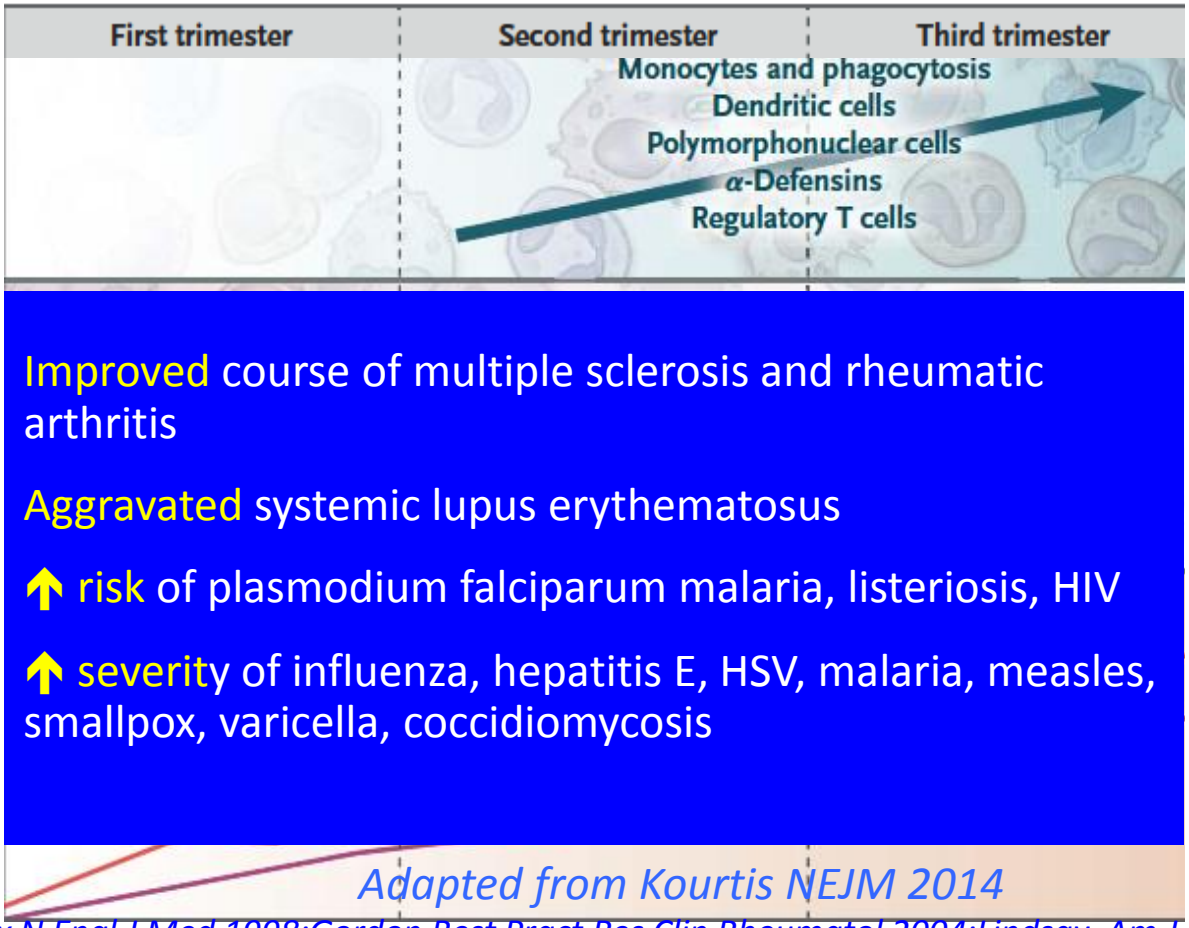
Does pregnancy or the postpartum period increase the risk of TB acquisition? reactivation? severity?

Pregnancy-associated immune changes are biologically significant

- Systemic immunomodulation that simultaneously embraces cellular immunosuppression, immunotolerance to various antigens, and enhanced inflammatory response.



Confavreux N Engl J Med 1998;Gordon Best Pract Res Clin Rheumatol 2004;Lindsay. Am J Epidemiol 2006; Diagne. Trans R Soc Trop Med Hyg 1997;Kumar. J Reprod Med 1997; Kourtis NEJM 2014

Common risk factors for progression of LTBI to disease

Risk Factor (study)	Relative risk % (95%CI)
Advanced, untreated HIV (Moss) (Pablos-Mendez)	 9.9 (8.7-11) 9.5 (3.6-25)
Close contact (Ferebee)	6.1 (5.5-6.8)
Chest Xray of untreated old healed TB (Ferebee)	5.2 (3.4-8.0)
Prednisone ≥ 15mg/d (Jick)	2.8 (1.7-4.6)
Chronic renal failure (Pablos-Mendez)	2.4 (2.1-2.8)
TNF-α inhibitor (Askling)	2.0 (1.1-3.5)
Poorly controlled Diabetes mellitus (Pablos-mendez)	1.7 (1.5-2.2)
Weight ≥ 10% below normal (Palmer)	1.6 (1.1-2.2)
Smoking (Bates)	1.5 (1.1-2,.2)
Pregnancy (Good, Carter, Espinal)	Limited data; mixed findings

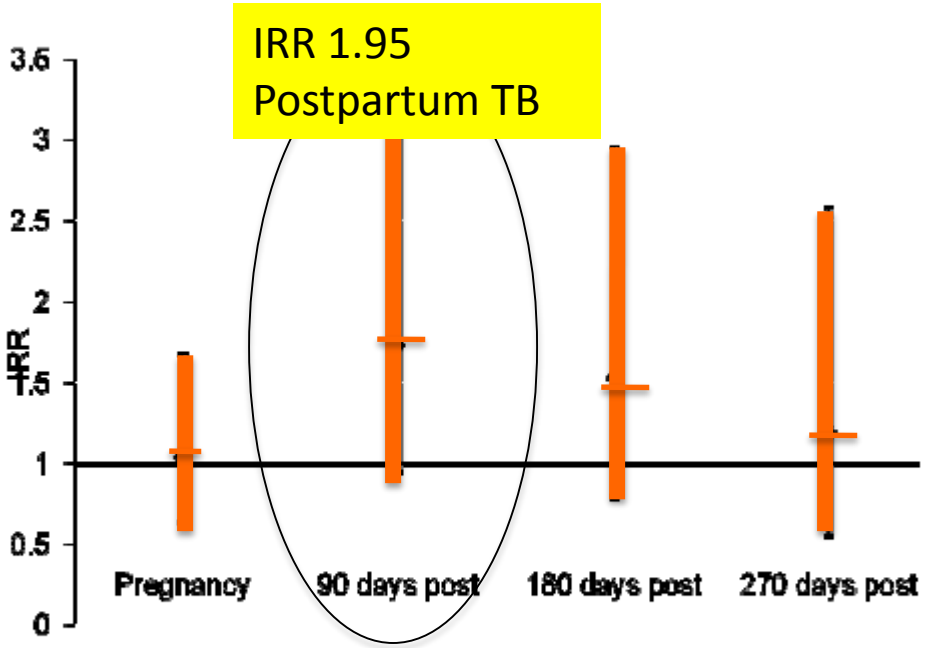
Horsburgh NEJM 2011, Good Am. J. Obstet. Gynecol 1981, Carter Chest 1994, Espinal JID 1996

Risk of TB in Pregnancy: UK primary care cohort

Impact on TB reactivation and severity debated

Clinical data limited and were not consistent or convincing
(*Good Am. J. Obstet. Gynecol 1981, Carter Chest 1994, Espinal 1996;Sterling 2007)*

Fig 2: Adjusted incidence rate ratios for different time periods



The adjusted incidence rate ratios for different pregnancy and post-partum periods from the self controlled case series model (adjusted for age and period). Bars denote 95% confidence intervals. Reference is the time outside of pregnancy (IRR 1), denoted by the x axis line

- 192,801 women enrolled 1996-2008
- with 264,136 pregnancies
- Mean f/up 9.1 years, 1,745,834 PY
- 177 TB events; postpartum
- 15.4 vs 9.1/100,000 PY

Zenner AJRCCM 2011

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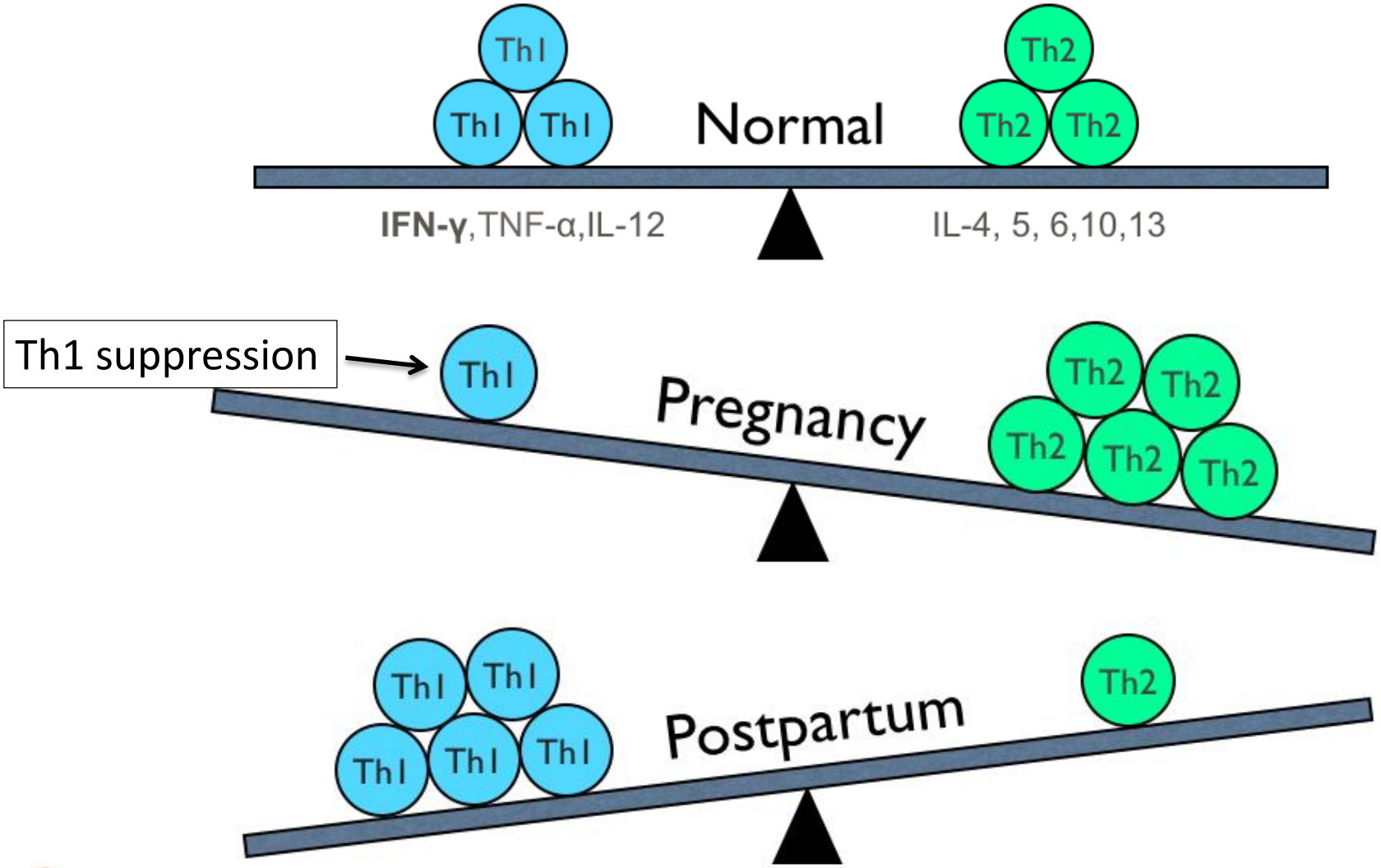
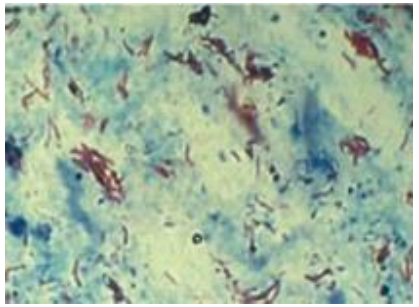
Biological plausibility? Immunology of pregnancy & TB



Adapted from Sykes, Mediators Inflamm 2012

Does pregnancy impact performance of screening for active or latent TB?



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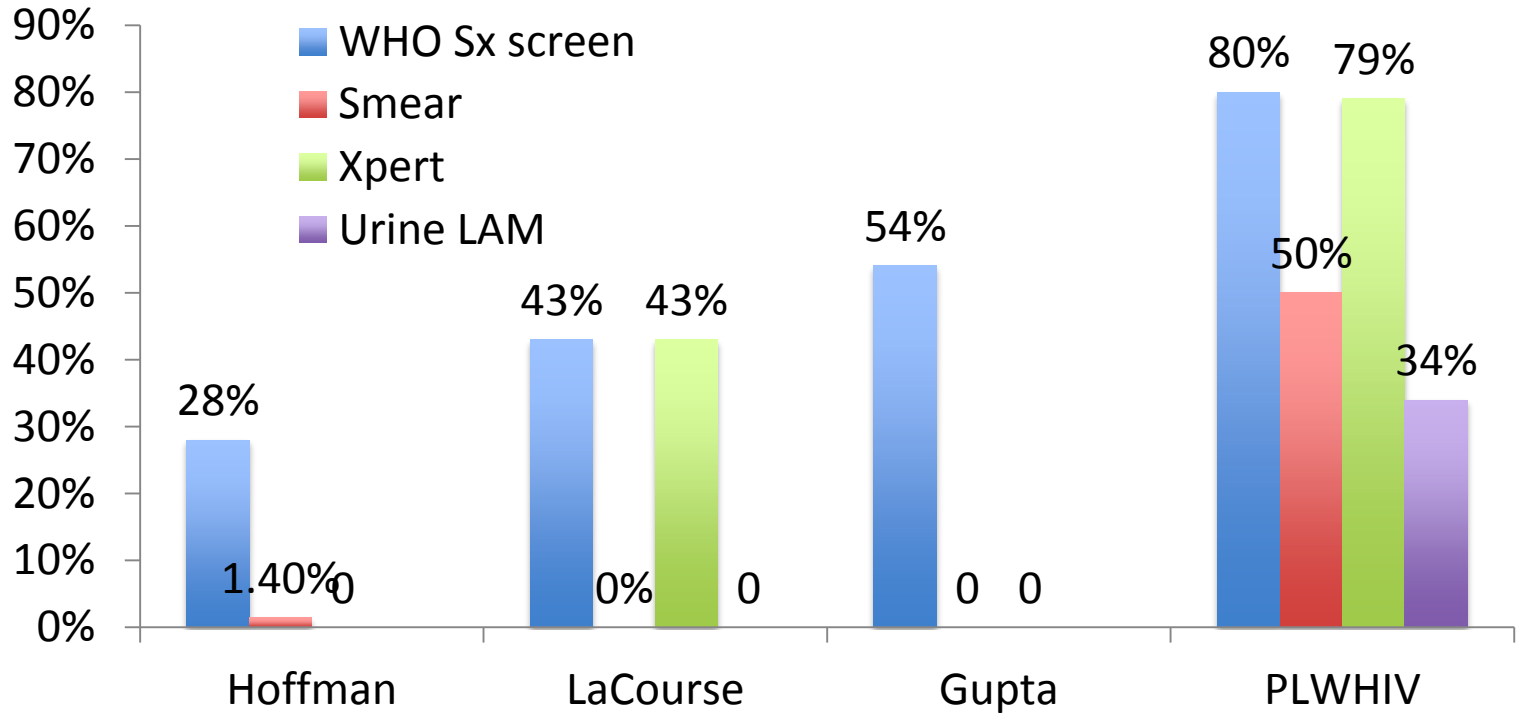
TB diagnostic sensitivity of WHO 4-symptom screen in pregnancy



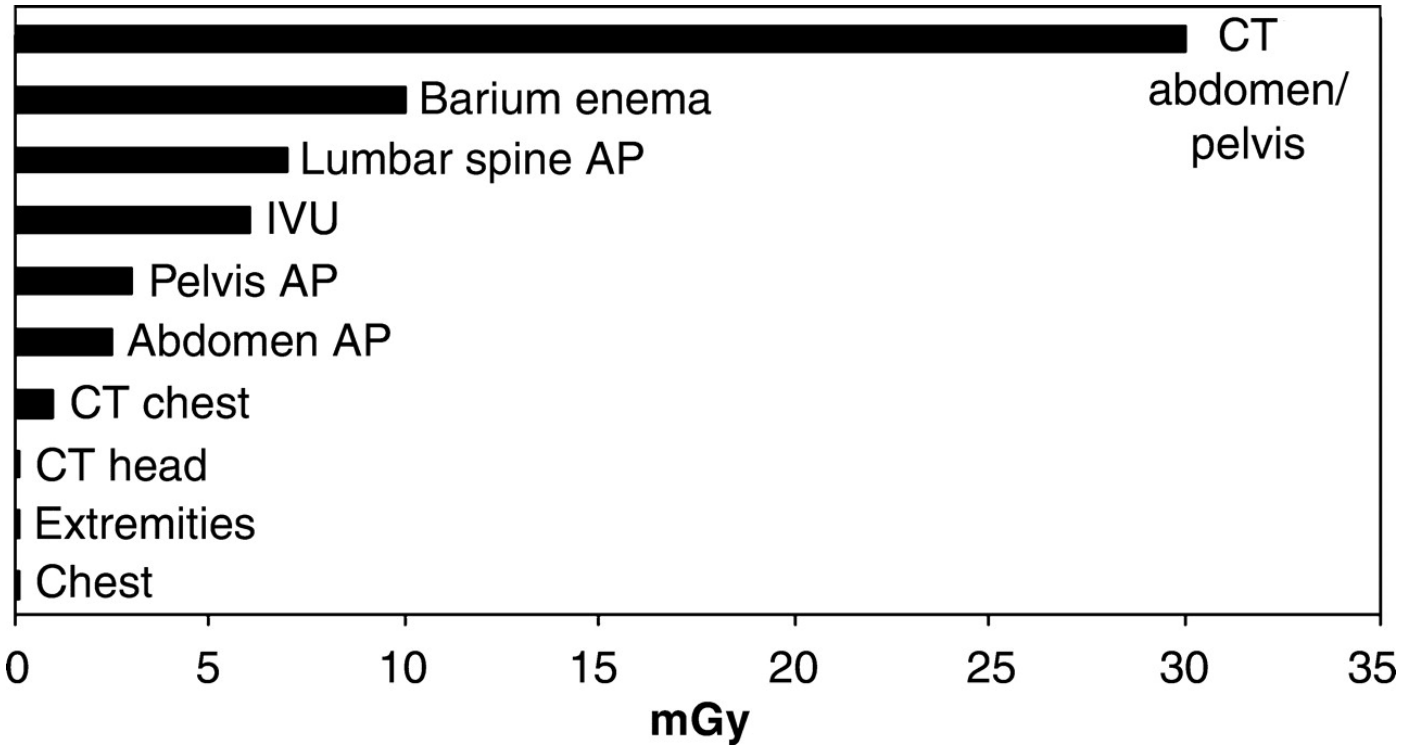
At least one WHO 4-symptom in 9-19% of women

Compared to non-pregnant HIV infected adults

- **Lower sensitivity observed but not clear if that is due to pregnancy alone**
- **High negative predictive value (NPV) BUT**
- **High prevalence of undiagnosed asymptomatic TB (HoffmanPLOS One 2013, #822)**

TIPS data courtesy of LaCourse and Cranmer, UW

Comparison of the estimated mean fetal absorbed dose from various radiographic and computed tomographic (CT) procedures



Patel, S. J. et al. Radiographics 2007;27:1705-1722
Radiological Society of North America, 2007

Screen for latent TB?

- Goal of Latent TB screening
  - Identify those at highest risk for reactivation disease
  - Target preventive therapy
- Implementation challenges
- Little attention paid to performance of latent TB diagnostics in pregnant/postpartum women in era of HIV
- Mixed data
  - Two US studies of IGRA (Quantiferon) test positivity was lower than TST (older age, foreign birth associated with positivity) *(Worjohol et al Obstet Gynecol 2011; Chebab Kansas J Med 2010)*
  - India, more Quantiferon positive than TST and discordance QGIT+/TST- was higher *(Mathad, PLOS One 2014)*
- Positive IGRA predictive of active TB postpartum (*Jonalagadda JID 2010, IJTLD 2013*

Prevalence of LTBI in US (TST)

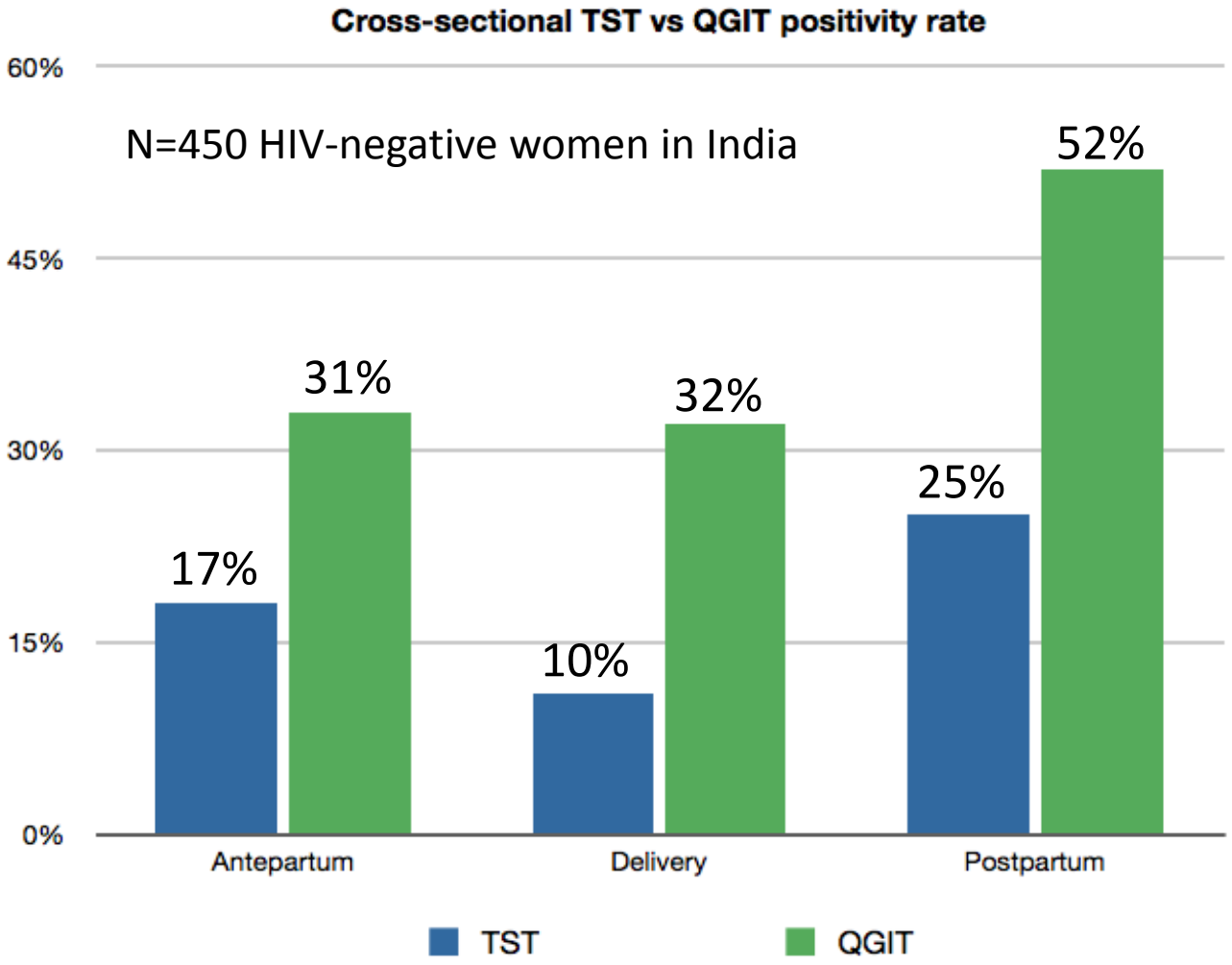
Group and Study	Expected prevalence % (95%CI)
US national sample (NHANES 2000)	4.2
Foreign born (Bennett)	18.7 (13.5-25.2)
Close contacts (Marks)	37.1 (35.7-38.5)
Homeless	
Kong	12.8 (12.2-13.5)
Moss	32.4 (30.5-34.4)
Injection drug users	
Riley	16.1 (12.5-22.4)
Grimes	27.7 (19.3-37.5)
Brassard	22.4 (17.7-28.5)
Salomon	14.0 (11.4-17.1)
Prisoners (Lobato)	17.0 (16.8-17.1)
US born, no other risk (Bennett)	1.8 (1.4-2.1)
Pregnant women	
Nolan (n=1621, LA)	
Mofenson (n=46,HIV+)	11.0
Schulte (n=176 HIV+ FL)	25.5
Sackoff (n=678 foreign born, NYC)	50.3

Horsburgh NEJM 2011; Nolan J Perinatol 1997;Schulte J Perinatol 2002; Mofenson Arch int Med 1995

TST vs IGRA: US studies

Publication	N	Sociodemo	trimester	results
Worjoloh Ob &Gyn 2011 San Fran	220 pregnant 199 had TST read	71% Hispanic 65% FB	71% 1st 22% 2nd 7% 3rd	45 discordant Kappa 0.26 (72% TST+/QGIT-) BCG at birth a/w TST+
Lighter-Fisher Ob &Gyn 2012 NYC	140 pregnant and 140 non-pregnant	79% Hispanic 41% FB 0 HIV+ 40% BCG 90% risk fctor for exp Mtb	31% 1st 15% 2nd 54% 3rd	21% TST+ 6% indeterminant 97% concordant negative Kappa 0.45 2%TST-/QGIT+
Chehab Kansan J Med 2010 Kansas	102 pregnant 50 non-pregnant	87% Hispanic	Not provided	3% concordant positive 88% concordant negative 9% discordant

TST vs IGRA positivity rates: When women screened and which latent TB diagnostic test used matters



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Mathad et al PLOS One 2014

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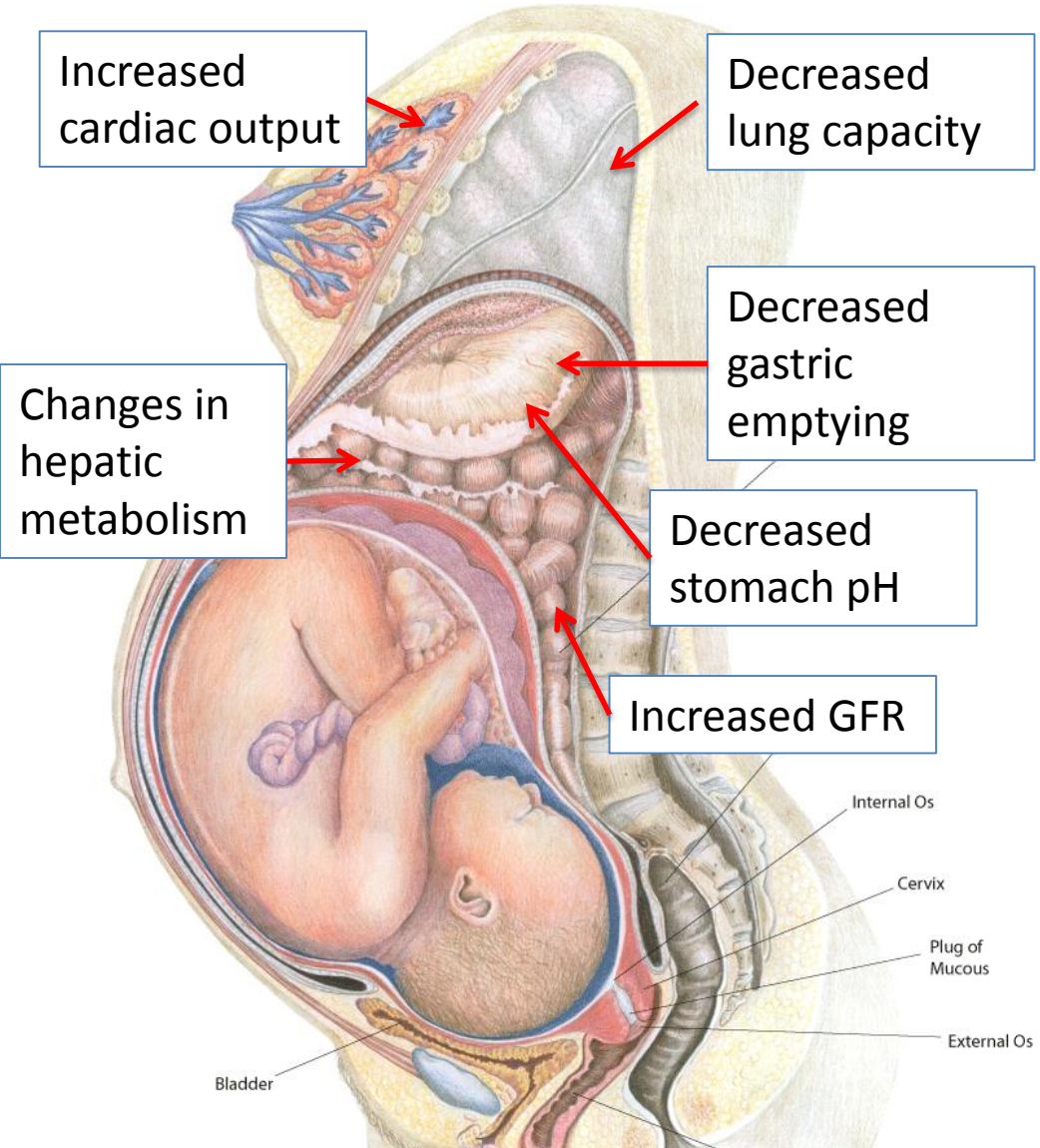
Does pregnancy impact TB treatment and prevention?

Physiology Changes of Pregnancy Can Significantly Impact Drug Metabolism, Safety and Efficacy



- Increased body fat
- Increased total body weight
- Decreased albumin
- Hepatic metabolism
  - Increased CYP3A4
  - Decreased CYP1A2 and CYP2C19

Frederiksen, Sem Perinatol 2001; Anderson, Clin Pharmacokinetics 2005

FDA Pharmaceutical Pregnancy Categories	
Category A	Adequate and well-controlled human studies demonstrate no risk.
Category B	Animal studies demonstrate no risk, but no human studies have been performed. OR Animal studies demonstrate a risk, but human studies have demonstrated no risk.
Category C	Animal studies demonstrate a risk, but no human studies have been performed. Potential benefits may outweigh the risks.
Category D	Human studies demonstrate a risk. Potential benefits may outweigh the risks.
Category X	Animal or human studies demonstrate a risk. The risks outweigh the potential benefits.

www.fda.gov

Importance of studying TB/HIV drugs in pregnancy: INH and EFV example

The population PK model post-hoc estimates were used to predict individual C_{min}

	Pre/intrapartum (n=73)	6 weeks Post-partum (n=75)
C_{min} (mg/L)*	1.35 (0.90-2.07)	2.00 (1.40-3.59)
% with C_{min}<1 mg/L	27%	13%

- Pregnancy modestly reduces EFV exposures, even after adjusting for weight, and proportion of women with EFV Cmin<1 mcg/mL higher in pregnancy than postpartum
  - especially in extensive CYP2B6 metabolizers
- TB treatment that includes INH and RIF doesn't reduce EFV concentrations, but EFV exposures higher in patients with slow NAT2 genotype taking INH
- No increased HIV MTCT noted

*Median (IQR)

Dooley et al., JID 2014 TSHIEPO study

First line drugs for TB in pregnancy

Drug	FDA	Crosses placenta	Breast-feeding	Issues in pregnant women
INH	C	Yes	Yes	Hepatotoxicity
Rifampin	C	Yes	Yes	Drug interactions with NVP, PIs, OCPs; may require Vit K
Rifabutin	B	Unk	Unk	Drug interactions with PIs, limited experience
EMB	B	Yes	Yes	
PZA	C	Unk	Unk	Different guidance

Brost Obstet Gyn Clin 1997;Bothamley Drug Safety 2001;Shin CID 2003; Micromedex; Mathad & Gupta CID 2012

Treatment of Active Pulmonary TB in Pregnancy

	Low Burden[1]	High Burden[2]
HIV negative	INH 5mg/kg/d x 9 mo RIF 10mg/kg/d x 9mo EMB wt-based x 2 mo B6 25mg/d x 9 mo	INH 5 mg/kg/d × 6 mo RIF 10 mg/kg/d × 6 mo EMB 15mg/kg/d x 2 mo **PZA 25mg/kg/d x 2 mo** B6 10-25mg/d x 6 mo
HIV positive	INH 300 mg/d × 6 mo RIF 600 mg/d × 6 mo EMB wt-based x 2mo **PZA wt-based × 2 mo** B6 25mg/d x 6 mo	INH 5 mg/kg/d × 6 mo RIF 10 mg/kg/d × 6 mo EMB 15mg/kg/d x 2 mo **PZA 25mg/kg/d x 2 mo** B6 10-25mg/d x 6 mo

LACTATION

CDC encourages breastfeeding if no longer infectious; WHO once smear negative

DIFFERENCE IN PZA guidance

1 CDC, ATS, IDSA guidelines
2 WHO, British thoracic Society, RNTCP and IUATLD guidelines

Treatment of EPTB involves same drugs but most experts recommend 9-12 mo for TBM (but include PZA plus steroids) or bone/joint infections

MDR TB in pregnancy

- Treatment guidelines similar to non-pregnant adults
  - Individualized treatment vs public health approach
  - At least 4 new agents
  - Favor injectable after delivery
  - Lactation little to no data so often not recommended
- >57 published case reports *(Gach 1999;Shin 2003; Nitta 1999;Lessnau 2003;Tabarsi 2007; Khan 2007; Palacios 2009; Toro 2011)*
  - 3 case series describes 4 cases HIV+ *(Khan 2007; Palacios 2009, Toro 2011)*
  - US, Italy, Peru, Iran, South Africa
- Regimens: variable
- Outcomes: case series suggest treatment success possible

Case

- 5 week old infant with HIV-infected mother presenting with failure to thrive
  - Delivered in the hospital without incident
    - Intrapartum Nevirapine given
    - HIV viral load negative
  - Had been gaining weight for first 2-3 weeks, but now fussy and weight has plateaued
  - No fever

Case

- Mother had developed cough at the end of the pregnancy but not productive, no fevers or shortness of breath
  - Cough has persisted and is now occasionally productive
  - No shortness of breath, but some fatigue
- SH: lives in an urban slum in a joint family setting (5 adults, 8 children); currently mother and child are staying with her mother in a nearby town
- FH: Husband died “from AIDS” during pregnancy; otherwise noncontributory

Treatment of TB in pregnancy

- Controversies:
  1. Drug-sensitive TB
     - CDC: Isoniazid, Rifampin, Ethambutol[1]
       - Continuation phase for 7 mos (total= 9mos)
     - WHO: Isoniazid, Rifampin, Ethambutol, Pyrazinamide[2]
       - CDC: Pyrazinamide only for HIV-infected (total=6 mos)
  2. MDR-TB: ????
     - Case series suggest good outcomes possible[3]
       - 23/38 Peruvian women with MDR-TB cured
       - 5 died, 2 treatment failure, 8 pregnancy complications
  3. HIV: EFV-based ART? PI-based ART?
     - Usually given EFV-based regimen

[1]CDC MMWR 2010; [2]WHO 2011; [3]Palacios CID 2009

FDA Categories of TB drugs

	Drug	FDA Category
First line therapy	Isoniazid	C
	Rifamycin	C
	Rifabutin	B
	Ethambutol	C
	Pyrazinamide	C
Second line therapy	Aminoglycosides	D
	Capreomycin	C
	Fluoroquinolones	C
	Ethionamide/Prothionamide	C
	Cycoserine	C
	PAS	C

* Bedaquiline= FDA Category B!

Follow-up and monitoring

- Consider checking LFTs monthly[1]
- Breast feeding allowed if on 1st line
  - NOT recommended with rifabutin or fluoroquinolones
  - No evidence for other medications
- If mother suspected of having TB, separate from infant[2]
  - Can resume when smear negative or infant started on TB treatment
  - Baby should get INH + BCG

[1]Blumberg AJRCCM 2003; [2]WHO 1998

Case

- Mother initiated on HRZE
- Baby given INH x 6 months
- Referred to DOTs center closer to home for follow-up
- Recommendation for household contact tracing…

Treatment as Prevention: The Case for Latent TB Treatment in Pregnancy

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Guidelines for Preventive TB Treatment in Pregnant Women

	Low Burden (US CDC)	High Burden (WHO)
Regimen	INH 300mg/d x 9 mo B6 25-50mg/d x 9 mo *OR* INH 900mg twice weekly x 9 mo B6 25-50mg/d x 9 mo	INH 300mg/d x 6 or 36 mo B6 10-25mg/d x 6 or 36 mo
HIV-negative	Defer for TST+ or IGRA+ until 2-3 mo postpartum unless known recent TB contact	No recommendations
HIV-positive	Immediate treatment for TST+ or IGRA+	Treatment for all HIV+ without active TB

CDC and ACOG recommendations

- Delay INH treatment until postpartum except if
  - HIV+
  - Recent TB contact
  - Recent TST conversion

MMWR 2000; Targeted Tuberculin testing and treatment of latent TB infection

Postpartum follow-up of LTBI is suboptimal

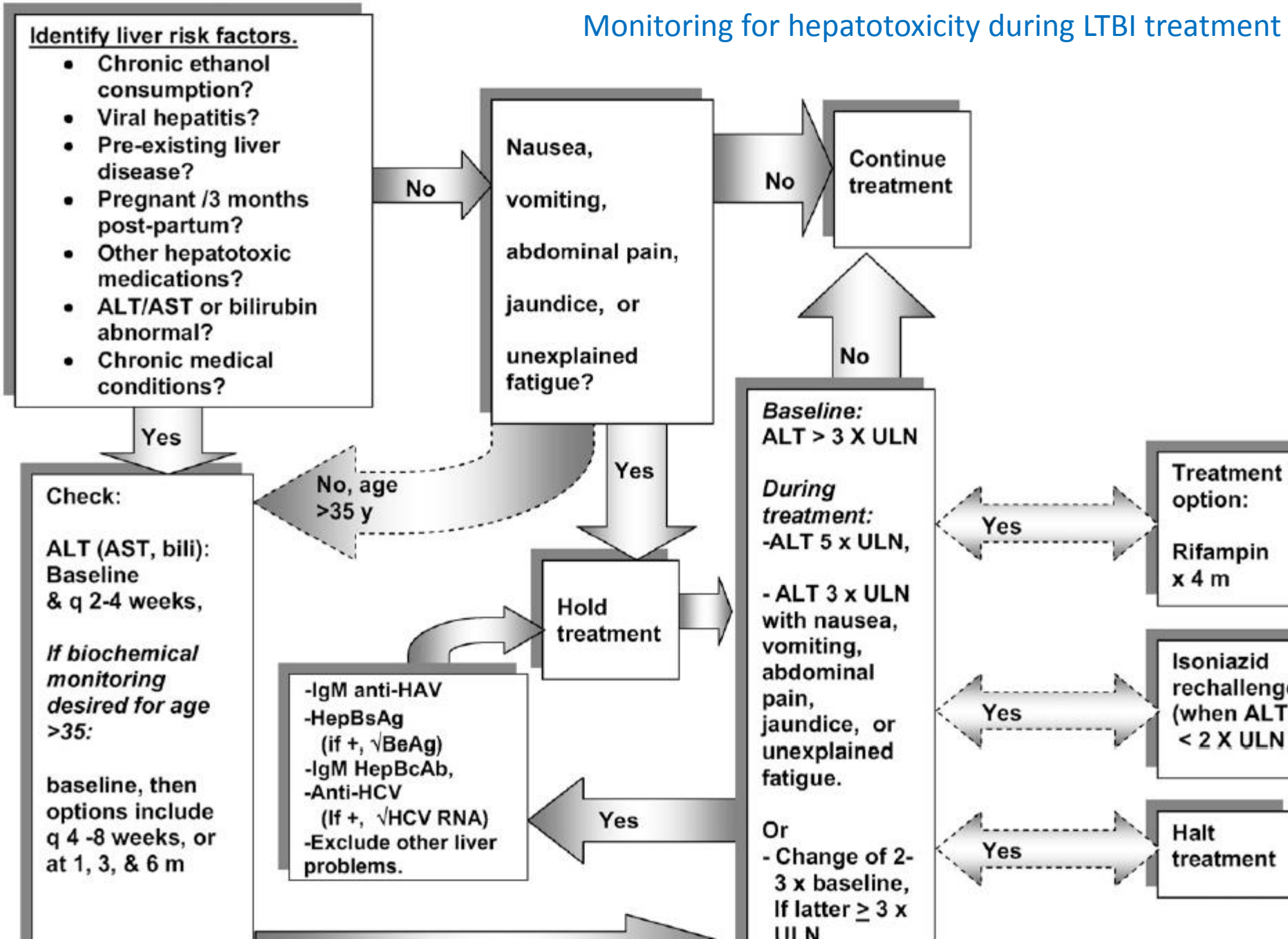
Cohort	SF, CA [1]	NY,NY [2]
N (%)	1331	730
TST+	32%	47%
Eligible for Tx	393	291
TB clinic follow-up	167 (47%)	50%
Completed Tx	71 (18%)	27 (9%)

[1]Cruz Am J Obstet Gyn 2005; [2]Sackoff Am J Obstet Gynecol 2006

Monitoring

- Prospective data lacking
- Most guidelines recommend baseline liver enzyme profiles
  - Underlying Liver disease
  - Pregnant or postpartum
  - Substantial alcohol consumption
  - Potentially hepatotoxic medications
- Monthly clinical symptom monitoring.
- Monthly monitoring of ALT likely unnecessary unless elevated baseline

Monitoring for hepatotoxicity during LTBI treatment



Challenges to LTBI screening and treatment

- Should all pregnant women be screened as TB prevalence continues to decrease in US?
- Data for IGRAs in pregnancy limited, cutoffs uncertain, no definition for conversion
- Newer shorter regimens being tested but pregnant women excluded

Selected Planned, On-going, and Recently Completed Randomized Clinical Trials for DS and DR TB

Prepared for the CDC Tuberculosis Trials Consortium *revised 24 April 2013*

Drug(s)	Trial Name	NCT Number	Arms	Ph	N	Group	Comments
High-dose Rifapentine - P - RPT							
	RIFAQUIN	SRCTN44153044	2MRZE/2M_2P_2 900 v. 2MRZE/4M_1P_1 1200 v. 2HRZE/4RH	III	1095	MRC/UK, EDCTP	Results CROI Mar 2013
	EDA Cape Town Trial	NCT00814671	2P_x (600 v. 450 mg) HZE v. 2HRZE	II	153	JHU (Dorman)	Results May 2013

>40 trials listed here that are planned, ongoing or recently completed

At least 8 are Phase III trials

All exclude pregnant women

More than 13 trials of preventive therapy in HIV-infected adults

INH for 6, 9, 12, 36 months

INH+ rifampin

INH+ rifapentine

INH+ ART

All excluded pregnant women

Akolo Cochrane metanalysis 2010; Sterling NEJM 2011; Martinson NEJM 2011; Samandari Lancet 2011; Rangaka Lancet ID 2014

AZD-5847 (Astra Zeneca)							
	n/a	NCT01516203	2 wk EBA 500 qd, 500 bid, 1200 qd, 800 bid v. RHZE	EBA	75	NIAID/DMID (Diacon)	Enrolling

Some TB trials and studies underway in pregnant women!

Treatment

- IMPAACT P1026s
  - PK/Safety of 1st line TB drugs with or without ARVs
- THSIEHPO (NICHD- Chaisson)
  - PK/safety of EFV/RIF, EFV/INH

Prevention

- IMPAACT P1078
  - TB APPRISE: Phase IV double blind RCT of antepartum vs postpartum INH for HIV+ pregnant women in high TB burden settings
- IMPAACT P2001
  - PK/safety of INH/rifapentine weekly for 12 weeks in HIV+ and HIV-
- ACTG/IMPAACT PHOENIX

  MDR contact prophylaxis

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IMPAACT
ACTG AIDS CLINICAL TRIALS GROUP
NIAID
NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development
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Towards Earlier Involvement of Pregnant Women in Trials of TB Drugs

May 2013 NIH sponsored workshop

Expert Consensus Statement forthcoming

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Prevention, Diagnosis, and Treatment of Tuberculosis in Children and Mothers: Evidence for Action for Maternal, Neonatal, and Child Health Services

Haileyesus Getahun, Delphine Sculier, Charalambos Sismanidis, Malgorzata Grzemska, and Mario Raviglione
Stop TB Department, World Health Organization, Geneva, Switzerland

Promoting joint policy and programming between TB, HIV and MCH

Key Programmatic actions:

- Integrated management of pregnancy and child health
- PMTCT
- Integrated Management of Child Illness (IMCI)
- Family planning
- TB and HIV

World Health Organization

Filling the gaps for maternal TB

Implementation Science
-PMTCT/TB screening &IPT

MOHs Lesotho, Kenya, South Africa
CDC, USAID, JHPIEGO, ICAP

Epidemiology of latent and active TB

NICHD TSHIEPO (CROI Abs#822 Cohn)
TIPS, India, Haiti studies,
IMPAACT PROMISE

ARVs /ATT drug interactions

A5388 (PK ARV, Rifampin, contraception)
NICHD TSHIEPO

Immunology and pathogenesis of TB

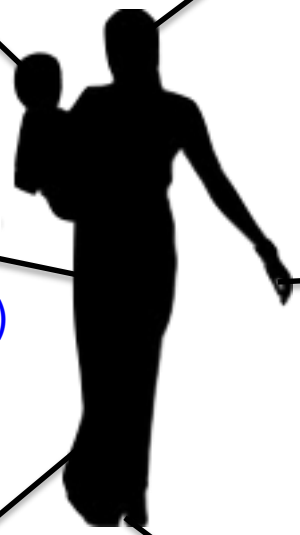
IMPAACT P1078
NICHD Pregnancy Immune Changes/TB

PK, safety, and outcome studies of:
-LTBI regimens
-1st and 2nd line TB medications

IMPAACT Pregnancy studies
P1078 (RCT of antepartum vs postpartum INH)
P2001 (PK, safety INH/rifapentine weekly)
P1026s (PK 1st line TB drugs and ARVs)
A5300/P2003 PHOENIX MDR contact

Cost-effectiveness studies for TB screening/treatment

CROI Abst# 1108 Shah



Summary

- Peak incidence of TB during reproductive age
- Maternal TB associated with adverse pregnancy outcomes, maternal mortality and infant TB and mortality
- Immune and physiological changes may be of importance to screening diagnostic yield, TB drug disposition
- Best approaches of integrated TB screening and prevention needed
- Need to include pregnant women in trials of diagnostics and drugs whenever feasible
- Several studies now ongoing that will help to fill in the knowledge gap

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